

L Number	Hits	Search Text	DB	Time stamp
1	1	disaccharide adj pyridinoline	USPAT; US-PGPUB; EPO; DERWENT	2003/05/14 08:43
2	5331636	s glucosyl adj galactosyl adj pyridinoline	USPAT; US-PGPUB; EPO; DERWENT	2003/05/14 08:44
3	4	glucosyl adj galactosyl adj pyridinoline	USPAT; US-PGPUB; EPO; DERWENT	2003/05/14 08:51
4	0	diglycoslated adj pyridinoline	USPAT; US-PGPUB; EPO; DERWENT	2003/05/14 08:52
5	1	pyr adj gal adj glc	USPAT; US-PGPUB; EPO; DERWENT	2003/05/14 08:53
6	1	diglycosylated adj pyridinoline	USPAT; US-PGPUB; EPO; DERWENT	2003/05/14 08:53

FILE 'CAPLUS, MEDLINE, BIOSIS, CA, SCISEARCH, EMBASE' ENTERED AT 08:35:09  
ON 14 MAY 2003

L1	0 S PRY (W) GAL (W) GLC
L2	0 S DIGLYCOSYLATED (W) PYRIDINOLINE
L3	0 S DISACCHARIDE (W) PYRIDINOLINE
L4	6461 S PYRIDINOLINE
L5	22 S GLUCOSYL (W) GALACTOSYL (W) PYRIDINOLINE
L6	6 DUPLICATE REM L5 (16 DUPLICATES REMOVED)

L6 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2003 ACS DUPLICATE 1  
 TI Search for new urinary biochemical markers of collagen degradation in man  
 AB Background: In the human body, collagen degrdn. produces various fragments released from the extracellular matrix, which end up in the urine as pyridinium cross-links, either free or bound to peptides or sugars. Methods: We developed a high-performance liq. chromatog. (HPLC) technique, which measures not only free pyridinoline (Pyr) and deoxypyridinoline (Dpyr), but also **glucosyl-galactosyl-pyridinoline** (glc-gal-pyr) and four still unidentified bound pyridinolines. Assuming that in Paget's disease of bone and in growing children the cross-links (CL) mainly originate from bone tissue, whereas after spinal cord injury their high excretion rather reflects the degrdn. of non-osseous collagen, we compared the urinary output of seven different cross-links, among which four had not been described before. Results: Our results show that one of those, which we called CL1, is essentially originating from bone and is more specific in this respect than Dpyr, whereas glc-gal-pyr also reflects the degrdn. of non-osseous collagen. The best indicator of non-bone collagen degrdn. was CL3, one of the newly discovered cross-links. Conclusions: In conclusion, we demonstrate that new sensitive pyridinoline cross-links can be identified and assayed in human urine and that their specificity helps to distinguish diseases related to bone collagen from those in which other forms of collagen are involved.

SO Clinica Chimica Acta (2003), 327(1-2), 81-86  
 CODEN: CCATAR; ISSN: 0009-8981  
 AU Roth, Marc; Uebelhart, Daniel

L6 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2003 ACS DUPLICATE 2  
 TI Association of baseline levels of urinary **glucosyl-galactosyl-pyridinoline** and type II collagen C-telopeptide with progression of joint destruction in patients with early rheumatoid arthritis  
 AB Objective. To evaluate whether measurements of urinary **glucosyl-galactosyl-pyridinoline** (Glc-Gal-PYD) and urinary C-terminal crosslinking telopeptide of type II collagen (CTX-II), 2 new markers of destruction of the synovium and cartilage collagen breakdown, resp., are assocd. with the progression of joint damage in patients with early rheumatoid arthritis (RA), and to compare this assocn. with that with serum matrix metalloproteinase 3 (MMP-3), a proteinase expressed by synovial tissue and chondrocytes, and that with serum C-reactive protein (CRP), an index of systemic inflammation. Methods. The prospective study cohort comprised 116 patients with early RA who were part of a large, double-blind, randomized study comparing the efficacy of etanercept and methotrexate. The relationship between baseline levels of urinary Glc-Gal-PYD, urinary CTX-II, and serum MMP-3 and the progression of joint destruction, as measured by changes in the modified Sharp score (av. findings of 2 independent readers) over 1 yr, was investigated. Results. Levels of urinary Glc-Gal-PYD (+70%), urinary CTX-II (+104%), and serum MMP-3 (+219%) were elevated compared with the levels in 76 healthy controls. The baseline levels of Glc-Gal-PYD ( $r = 0.30$ ), CTX-II ( $r = 0.25$ ), and MMP-3 ( $r = 0.29$ ) correlated with the changes over 1 yr in the total Sharp score (joint space narrowing and bone erosion). Patients with baseline levels of Glc-Gal-PYD, CTX-II, and MMP-3 that were higher than the mean + 2 SD in healthy controls had a significantly greater progression of joint damage, with an increase in the total Sharp score over 1 yr that was from 3- to 8-fold higher than that in patients with low baseline levels of these markers. Moreover, patients with these higher levels of Glc-Gal-PYD, CTX-II, and MMP-3 had a higher risk of progression of the disease (increase in total Sharp score  $\geq 0.5$  units) than did the other patients (relative risks and 95% confidence intervals [95% CI] 3.3 [95% CI 1.5-7.4], 2.5 [95% CI 1.1-5.7], and 2.5 [95% CI 1.1-5.6],

resp.). The baseline serum level of CRP was not significantly assocd. with the progression of joint damage. Adjustment of the levels of Glc-Gal-PYD, CTX-II, and MMP-3 according to radiol. damage at baseline did not alter their assocn. with progression. After adjustment for serum CRP, the relative risk slightly decreased, but remained significant, for Glc-Gal-PYD (2.6 [95% CI 1.1-6.3]). Patients with both increased levels of the mol. markers and radiol. damage at baseline had a higher risk of progression of joint damage than did those with either high mol. marker levels or radiol. damage. Conclusion. High baseline levels of Glc-Gal-PYD, CTX-II, and MMP-3 are assocd. with increased risk of progression of joint destruction over 1 yr in early RA. The assocn. between baseline levels of urinary Glc-Gal-PYD and progression of joint erosion was independent of the severity of radiol. damage and inflammation at baseline. Combining the measurements of these mol. markers with radiol. assessment of joint damage may be useful for identifying patients with RA who are at high risk of rapid progression and for whom early aggressive treatment would be beneficial.

SO Arthritis & Rheumatism (2002), 46(1), 21-30

CODEN: ARHEAW; ISSN: 0004-3591

AU Garnero, Patrick; Gineyts, Evelyne; Christgau, Stephan; Finck, Barbara; Delmas, Pierre D.

L6 ANSWER 3 OF 6 MEDLINE

DUPLICATE 3

TI Cross sectional evaluation of biochemical markers of bone, cartilage, and synovial tissue metabolism in patients with knee osteoarthritis: relations with disease activity and joint damage.

AB OBJECTIVE: To analyse the relations between the urinary levels of type II collagen C-telopeptide (CTX-II) and **glucosyl-galactosyl pyridinoline** (Glc-Gal-PYD)-two newly developed biochemical markers of type II collagen and synovial tissue destruction respectively-disease activity and the severity of joint destruction in patients with knee osteoarthritis (OA). The clinical performance of these two new markers was compared with that of a panel of other established biochemical markers of connective tissue metabolism. METHODS: The following biochemical markers were measured in a group of 67 patients with knee OA (mean age 64 years, median disease duration eight years ) and in 67 healthy controls: for bone, serum osteocalcin, serum and urinary C-telopeptide of type I collagen (CTX-I); for cartilage, urinary CTX-II, serum cartilage oligomeric matrix protein (COMP), and serum human cartilage glycoprotein 39 (YKL-40); for synovium, urinary Glc-Gal-PYD, serum type III collagen N-propeptide (PIIINP), serum hyaluronic acid (HA); and for inflammation, serum C reactive protein. Biochemical markers were correlated with pain and physical function (WOMAC index) and with quantitative radiographic evaluation of the joint space using the posteroanterior view of the knees flexed at 30 degrees. RESULTS: All bone turnover markers were decreased in patients with knee OA compared with controls (-36%, -38%, and -52%,  $p < 0.0001$  for serum osteocalcin, serum CTX-I and urinary CTX-I, respectively). Serum COMP (+16%,  $p = 0.0004$ ), urinary CTX-II (+25%,  $p = 0.0009$ ), urinary Glc-Gal-PYD (+18%,  $p = 0.028$ ), serum PIIINP (+33%,  $p < 0.0001$ ), and serum HA (+ 233%,  $p < 0.0001$ ) were increased. By univariate analyses, increased urinary Glc-Gal-PYD ( $r = 0.41$ ,  $p = 0.002$ ) and decreased serum osteocalcin ( $r = -0.30$ ,  $p = 0.025$ ) were associated with a higher total WOMAC index. Increased urinary CTX-II ( $r = -0.40$ ,  $p = 0.0002$ ) and Glc-Gal-PYD ( $r = -0.30$ ,  $p = 0.0046$ ) and serum PIIINP ( $r = -0.29$ ,  $p = 0.0034$ ) were the only markers which correlated with joint surface area. By multivariate analyses, urinary Glc-Gal-PYD and CTX-II were the most important predictors of the WOMAC index and joint damage, respectively. CONCLUSION: Knee OA appears to be characterised by a systemic decrease of bone turnover and increased cartilage and synovial tissue turnover. CTX-II, Glc-Gal-PYD, and PIIINP may be useful markers of disease severity in patients with knee OA.

SO ANNALS OF THE RHEUMATIC DISEASES, (2001 Jun) 60 (6) 619-26.

Journal code: 0372355. ISSN: 0003-4967.

AU Garnero P; Piperno M; Gineyts E; Christgau S; Delmas P D; Vignon E

L6 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2003 ACS DUPLICATE 4

TI Urinary excretion of **glucosyl-galactosyl pyridinoline**: a specific biochemical marker of synovium degradation

AB **Glucosyl-galactosyl pyridinoline**

(Glc-Gal-PYD), which has been identified in urine, is a glycosylated analog of pyridinoline. The tissue distribution of this mol. has not been yet detd. and its utility as a potential biochem. marker of joint degrdn. in patients with joint diseases has not been investigated. In this study, we demonstrate that Glc-Gal-PYD is abundant in human synovium tissue, absent from bone and present in minute amts. in cartilage and other soft tissues, such as muscle and liver. Using an ex vivo model of human joint tissue degrdn., we found that Glc-Gal-PYD is released from synovium tissue, but not from bone and cartilage. The urinary level of Glc-Gal-PYD was increased by 109% in patients with rheumatoid arthritis (RA) compared with healthy adults, but was normal in patients with Paget's disease of bone. In addn., Glc-Gal-PYD was higher in those patients with destructive disease, as assessed by X-rays of the joints, than in those with non-destructive RA. Glc-Gal-PYD may be useful for the clin. investigation of patients with joint disease.

SO Rheumatology (Oxford, United Kingdom) (2001), 40(3), 315-323

CODEN: RUMAFK; ISSN: 1462-0324

AU Gineyts, E.; Garnero, P.; Delmas, P. D.

L6 ANSWER 5 OF 6 SCISEARCH COPYRIGHT 2003 THOMSON ISI

TI Urinary **glucosyl-galactosyl pyridinoline** - A new specific marker of synovium turnover-predicts progression of joint damage in early rheumatoid arthritis.

SO ARTHRITIS AND RHEUMATISM, (SEP 2000) Vol. 43, No. 9, Supp. [S], pp. 2014-2014.

Publisher: LIPPINCOTT WILLIAMS & WILKINS, 530 WALNUT ST, PHILADELPHIA, PA 19106-3621.

ISSN: 0004-3591.

AU Garnero P (Reprint); Gineyts E; Peterfy C; Finck B; Delmas P D

L6 ANSWER 6 OF 6 SCISEARCH COPYRIGHT 2003 THOMSON ISI

TI **Glucosyl-galactosyl pyridinoline**: A specific biochemical marker of synovium degradation.

SO ARTHRITIS AND RHEUMATISM, (SEP 2000) Vol. 43, No. 9, Supp. [S], pp. 717-717.

Publisher: LIPPINCOTT WILLIAMS & WILKINS, 530 WALNUT ST, PHILADELPHIA, PA 19106-3621.

ISSN: 0004-3591.

AU Gineyts E (Reprint); Garnero P; Delmas P D

=>